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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1632	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File

Office Action Summary	Application No.	Applicant(s)	
	09/479,467	STERNBERG ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on *11 September 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-92* is/are pending in the application.

4a) Of the above claim(s) *2,4,6,8,12-14,18-20,23-24,33-40,43-48,50-73,78-81, and 84-92* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5,7,9-11,15-17,21-22,25-32,41-42,49,74-77,and 82-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15)☒ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of group I, claims 1,3, 5, 7, 9-11, 15-17, 21-22, 25-32, 41-42, 49, 74-77, and 82-84 in Paper No. 13 is acknowledged. The traversal is on the ground(s) that the Examiner has not shown serious search burden would be required to search all the claims. Applicants argue that it would not have been undue to search the claims from groups I and XI, II and XII, andI-II and VI-X This is not found persuasive because it is maintained that each of the inventions requires a separate search status. In particular, Group I, directed to nucleic acids, vectors, and transgenic nematodes are not used in the screening methods of Group X, which requires mutagenizing wild-type nematode. As such, the Invention of Group X requires materially different reagents and technical considerations than methods employing the nucleic acids, vectors and host cells of Group I. Also the nucleic acid molecules of Groups I and II have different structures and encode proteins that have different functions. Further, the Invention of Group I may be used for materially different methods than the methods of Groups VI-X. For example, nucleic acids of Group I may be used hybridization protocols. Therefore, it is maintained that these inventions are distinct due to their divergent subject matter and are thus, separately classified and searched.

The requirement is still deemed proper and is therefore made FINAL.

Please note that after a final requirement for restriction, the Applicants, in addition to making any response due on the remainder of the action, may petition the Commissioner to review the requirement. Petition may be deferred until after final action on or allowance of claims to the invention elected, but must be filed not later than appeal. A petition will not be considered if reconsideration of the requirement was not requested. (See § 1.181.).

Claims 1-24 are pending, however, claims 2, 4, 6, 8, 12-14, 18-20, 23-24, 33-40, 43-48, 50-73, 78-81, and 85-92 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions, the requirement having been traversed in Paper No. 12.

Claim Objections

Claims 82-84 are objected to because of the following informalities: claim 82 depends from non-elected claim 78. Claims 83-84 depend from claim 82. Appropriate correction is required.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1,3,5,9-11, 15-17, 21-22, 25-32, 41-42, 49, 74-77, and 82-84 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is directed to an isolated nucleic acid molecule comprising the nucleotide sequence set forth in Seq Id 3, the complement of nucleotide sequence of Seq Id 3, a nucleotide sequence that hybridizes to the nucleotide sequence of Seq Id 3, and that is present in the genome of a nemotode, or a degenerate nucleotide sequence of Seq Id 3. Claim 3 is directed to the same nucleotide sequence that encodes a LOV-1 protein from a nematode. Claim 5 is directed to the same nucleic acid molecule wherein the nucleic acid molecule encodes the amino acid sequence set forth in Seq Id 4. Claim 7 is directed to the same nucleic acid molecule wherein the nucleic acid molecule is derived from C. elegans. Claim 9 is directed to an isolated gene comprising the nucleic acid molecule of claim 1. Claims 10-11 are directed to the same gene wherein the gene comprises transcriptional control sequences that are homologous or heterologous to the encoded gene. Claims 15-17 are directed to isolated nucleic acid molecules that encode mutant forms of the protein of claim 3. Claim s 21-22 are directed to a construct comprising the nucleic acid molecule of claim 1 wherein the nucleic acid molecule is operably linked to a reporter construct, particularly the green fluorescent protein. Claims 25-26 are directed to an expression vector that comprises the nucleic acid molecule of claim 1. Claims 27-28 are directed to a transgenic nematode comprising

the vector of claim 26, wherein the vector is maintained extrachromosomally. Claims 30-32 are directed to the same transgenic nematode, wherein the vector further comprises a reporter gene, and particularly wherein the nucleic acid molecule contained within the vector encodes a mutant protein. Claims 41-42 are directed to an isolated nucleic acid molecule encoding a mutant LOV-1 protein and a transgenic nematode comprising the same nucleic acid molecule. Claim 49 is directed to an isolated nucleic acid molecule of claim 22 that encodes the sequence of amino acids set forth in Seq Id 15. Claims 74-77 are directed to a method of identifying genes or regulatory factors involved in polycystic kidney diseases using transgenic nematodes that comprising LOV-1 transgenes that have been mutagenized. Claims 82-84 are directed a method of using mutant nematodes for identifying genes.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed. "*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

While the specification provides adequate written description for the claimed invention (methods and products) only with regard to the nucleic acid sequence set forth in Seq Id 3 isolated from *C. elegans*, nucleic acid molecules that encode the amino acid sequences set forth in Seq Ids 4 and 15, and mutant *C. elegans* that comprises a

mutated LOV-1 gene exhibiting a phenotype of defective mating behavior (particularly in the male sensory behaviors response and location of vulva), the specification fails to describe the other nucleic acid molecules that are mutants of Seq Id 3, other nucleic acid molecules that hybridize to Seq Id 3, nucleic acid molecules that encode mutant LOV-1, any gene that comprises the nucleic acid sequence of Seq Id 3, any and all homologs of Seq Id 3 isolated from any and all nematodes, any and all transgenic nematodes that comprise a vector that comprises the nucleotide sequence of Seq Id 3, any and all transgenic nematodes that comprise a vector that comprises a nucleotide sequence that encodes a mutant protein, any and all transgenic nematodes that comprise a nucleotide sequence that encodes for a mutant LOV-1 protein, any and all transgenic nematodes that have been mutagenized for use in methods of identifying gene or regulators involved in polycystic kidney disease or that interact with LOV-1, or any other mutant nematode without any described phenotype, encompassed in the claims with particularity to indicate that Applicants had possession of the claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant

case, the claimed embodiments of any and all species of nucleic acid molecules within the genus of nucleic acid molecules of Seq Id 3, any gene comprising any species nucleic acid of Seq Id 3 molecule, any and all transgenic nematodes comprising a vector that contains either a wild-type or mutant nucleic acid molecule of the nucleotide sequence set forth in Seq Id 3 or any transgenic nematode that comprises a nucleic acid molecule that encodes a mutant LOV-1 protein [other than the nucleic acid sequence set forth in Seq Id 3 isolated from *C. elegans*, nucleic acid molecules that encode the amino acid sequences set forth in Seq Ids 4 and 15, and mutant *C. elegans* that comprises a mutated LOV-1 gene exhibiting a phenotype of defective mating behavior (particularly in the male sensory behaviors response and location of vulva], lack a written description. The specification fails to describe what nucleotide sequence other than the nucleotide sequence set forth in Seq Id 3, fall into this genus when and constructed and used as claimed or any phenotype that is correlatable with the expression of the nucleotide sequence set forth in Seq Id 3, and it was unknown as of Applicants' effective filing date that any of these nucleic acid molecules would have the properties of the nucleotide sequence set forth in Seq Id 3, particularly with regard to the male sensory behaviors response and location of vulva in *C. elegans* or could produce any relevant correlatable phenotype when expressed in a transgenic nematode. The skilled artisan cannot envision the detailed chemical structure of all of the encompassed nucleotide sequences within the genus of the nucleotide sequence set forth in Seq Id 3 or any correlatable phenotypes of any and all transgenic nematode comprising a vector that comprises any Seq Id 3 nucleic acid molecule or any nucleic

acid molecule that encodes for a mutant LOV-1 protein, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only the described nucleic acid sequence set forth in Seq Id 3 isolated from *C. elegans*, nucleic acid molecules that encode the amino acid sequences set forth in Seq Ids 4 and 15, and mutant *C. elegans* that comprises a mutated LOV-1 gene exhibiting a phenotype of defective mating behavior (particularly in the male sensory behaviors response and location of vulva) meet the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 27-32, 42-42, 49, 74-77, and 82-84 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a mutant *C. elegans* that

comprises mutant LOV-1 gene exhibiting a phenotype of defective mating behavior particularly in the male sensory behaviors response and location of vulva, does not reasonably provide enablement for any and all transgenic nematodes comprising a vector encoding the nucleic acid sequence set forth in Seq Id 3, or any species of the nucleic acid sequence set forth in Seq Id 3, or any nucleic acid that encodes a mutated LOV-1 protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 27-28 are directed to a transgenic nematode comprising the vector of claim 26, wherein the vector is maintained extrachromosomally. Claims 30-32 are directed to the same transgenic nematode, wherein the vector further comprises a reporter gene, and particularly wherein the nucleic acid molecule contained within the vector encodes a mutant protein. Claims 41-42 are directed to an isolated nucleic acid molecule encoding a mutant LOV-1 protein and a transgenic nematode comprising the same nucleic acid molecule. Claim 49 is directed to an isolated nucleic acid molecule of claim 22 that encodes the sequence of amino acids set forth in Seq Id 15. Claims 74-77 are directed to a method of identifying genes or regulatory factors involved in polycystic kidney diseases using transgenic nematodes that comprising LOV-1 transgenes that have been mutagenized. Claims 82-84 are directed a method of using mutant nematodes for identifying genes.

The specification discusses that the invention features an animal model for studying the etiology of polycystic kidney disease and identifying genes and factors

involved in the disease pathway. See page 1, 2nd paragraph. The specification discusses that the invention features a mutagenized *C. elegans* comprising a mutated LOV-1 gene exhibiting a phenotype of defective mating behavior particularly in the male sensory behaviors response and location of vulva. See pages 51-52. The specification also discusses that the phenotype of defective mating behavior particularly in the male sensory behaviors response and location of vulva can be rescued when mutant *C. elegans* are injected with a vector comprising the nucleotide sequence set forth in Seq Id 3. See page 52. While the specification provides extensive teachings pertaining to the isolation and characterization of the LOV-1 nucleic acid sequence (Seq Id 3) and mutagenized *C. elegans*, the specification fails to provide any relevant teachings or specific guidance with regard to the generation of any and all transgenic nematodes comprising a transgene comprising a LOV-1 nucleic acid molecule, in particular an animal which expresses (or overexpresses) the transgene such that a disease phenotype occurs (as is consistent with the discussion of the specification). Furthermore, the specification fails to even describe any particular phenotype exhibited by a transgenic nematode, (other than a transgenic mutant *C. elegans* that has been rescued of the defective mating behavior phenotype, particularly in the male sensory behaviors response and location of vulva) of the invention, only that such an animal would be useful as a disease model (for drug screening, or identifying other genes that regulate or are regulated by LOV-1). Thus, as enablement requires the specification to teach how to make and use the claimed invention, the specification fails to enable the production of any transgenic nematode for use as a model for studying the etiology of

polycystic kidney disease and identifying genes and factors involved in the disease pathway.

[Note that although the claimed transgenic nematodes are not limited to expression of the transgene at a level resulting in a correlatable phenotype, with regard to claim breadth, the standard under 35 U.S.C. §112, first paragraph, entails the determination of what the claims recite and what the claims mean as a whole. In addition, when analyzing the enabled scope of the claims, the teachings of the specification are to be taken into account because the claims are to be given their broadest reasonable interpretation that is consistent with the specification. As such, the broadest reasonable interpretation of the claimed transgenic nematode having cells which harbor LOV-1 transgene is one that expresses the transgene at a level sufficient to result in a correlatable phenotype (i.e., it is unknown what other purpose the transgenic nematode would serve if the transgene is not expressed at a sufficient level for a resulting correlatable phenotype).]

As the specification fails to provide any relevant teachings or guidance with regard to the production of any transgenic nematode as claimed, one of skill would not be able to rely on the state of the transgenic art for an attempt to produce LOV-1 transgenic nematodes. This is because the state of the art of transgenics is not a predictable art with respect to transgene behavior and the resulting phenotype. While the state of the art of transgenics is such that one of skill in the art would be able to produce transgenic animals comprising a transgene of interest; it is not predictable if the transgene would be expressed at a level and specificity sufficient to cause a particular

phenotype. For instance, the level and specificity of expression of a transgene as well as the resulting phenotype of the transgenic animal are directly dependent on the specific transgene construct. The individual gene of interest, promoter, enhancer, coding, or non-coding sequences present in the transgene construct, the specificity of transgene integration into the genome, for example, are all important factors in controlling the expression of a transgene in the production of transgenic animal which exhibits a resulting phenotype. This observation is supported by Wall (Theriogenology, 1996) who states that "[o]ur lack of understanding of essential genetic control elements makes it difficult to design transgenes with predictable behavior." See page 61, last paragraph. See also Houdebine (Journal of Biotechnology, 1994) who discloses that in the field of transgenics, constructs must be designed case by case without general rules to obtain good expression of a transgene (page 275, column 1, 1st paragraph); e.g., specific promoters, presence or absence of introns, etc. As such guidance is lacking in the instant specification, it fails to feature any correlation between the over-expression of a LOV-1 transgene and a specific resulting disease phenotype.

Furthermore, without evidence to the contrary, transgene expression in different species of transgenic non-human animals is not predictable and varies according to the particular host species, and specific promoter/gene combination(s). This observation is specifically supported by Hammer et al. (Journal of Animal Science, 1986) who report the production of transgenic mice, sheep and pigs; however only transgenic mice exhibited an increase in growth due to the expression of the gene encoding human growth hormone (pages 276-277, Subsection: Effect of Foreign GH on Growth). The

same transgene construct in transgenic pigs and sheep did not cause the same phenotypic effect. See also Ebert et al. (Molecular Endocrinology, 1988). This observation is supported by Mullins et al. (Journal of Clinical Investigations, 1996) who report on transgenesis in the rat and larger mammals. Mullins et al. state that "a given construct may react very differently from one species to another." See page S39, Summary. Wall et al. report that "transgene expression and the physiological consequences of transgene products in livestock are not always predicted in transgenic mouse studies." See page 62, first paragraph. Kappel et al. (Current Opinion in Biotechnology, 1992) disclose the existence of inherent cellular mechanisms that may alter the pattern of gene expression such as DNA imprinting, resulting from differential CpG methylation (page 549, column 2, 3rd full paragraph). Strojek and Wagner (Genetic Engineering, 1988) pointed out that a high degree of expression of a transgene in a mouse is often not predictive of high expression in other species, including pigs and rabbits, because, for example, the cis acting elements may interact with different trans-acting factors in these other species (paragraph bridging pages 238-239). Given such species differences in the expression of a transgene, particularly when taken with the lack of guidance in the specification for the production of any and all transgenic nematodes whose genome comprises a LOV-1 transgene, it would have required undue experimentation to predict the results achieved in any one host animal comprising and expressing a LOV-1 transgene, the levels of the transgene product, the consequences of that production, and therefore, the resulting phenotype.

Therefore, in view of the quantity of experimentation necessary to determine the parameters listed above for the production of transgenic LOV-1 nematodes, the lack of direction or guidance provided by the specification for the production of any transgenic LOV-1 expressing a transgene encoding LOV-1 for use of the nematode as a model for studying the etiology of polycystic kidney disease and identifying genes and factors involved in the disease pathway, the absence of working examples for the demonstration or correlation to the production of a transgenic animal expressing a transgene encoding LOV-1 for use of the animal as a model for studying the etiology of polycystic kidney disease and identifying genes and factors involved in the disease pathway, in particular when the transgene comprises LOV-1 coding sequences under the control of any and all promoters, and more particularly when the expression of the transgene must occur at a level resulting in a corresponding phenotype, and the unpredictable state of the art with respect to transgene behavior in transgenic animals of any and all species, it would have required undue experimentation for one skilled in the art to make and/or use the claimed invention. **Note, if a nexus can be shown between expression of a LOV-1 transgene and a correlatable phenotype in a transgenic *C. elegans* then the enablement rejection over the transgenic nematode will be changed to a scope of enablement. Also, for the claims to be considered to be in allowable form the specific phenotype that correlates to expression of the LOV-1 transgene must be included in the claim.**

Claims 1, 3, 5, 9-11, 15-17, 21-22, 25-32, 41-42, and 49 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the nucleotide sequence set forth in Seq Id 3 isolated from *C. elegans*, does not reasonably provide enablement for any and all homologs of Seq Id 3 isolated from any and all nematodes, any and all mutant forms of Seq Id 3, or any gene comprising the nucleotide sequence set forth in Seq Id 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With regard to claims, 1, 3, 5, 9-11, 15-17, 21-22, 25-32, 41-42, and 49 these claims are broadly drawn to any and all homologs of Seq Id 3 isolated from any and all species of nematode, of which only *C. elegans* has been delineated in the specification, and any and all mutant forms of Seq Id 3. The specification fails to provide parameters, for which one skilled in the art could reasonably isolate homologs of Seq Id 3 from other nematodes or mutant forms of Seq Id 3 which exist in the art can be utilized to make or practice the claimed invention without undue experimentation, particularly in view of the absence of guidance provided by the specification as to the isolation of homologs of Seq Id 3 from other nematode species and in view of the lack of guidance provided by the specification with regard to the degree of homology of homologs of Seq ID 3 from other nematode species. As such, the claims are only enabled for the nucleotide sequence set forth in Seq Id 3 isolated from *C. elegans*.

Accordingly, in view of the quantity of experimentation necessary to determine the parameters listed above, the lack of direction or guidance provided by the

specification to isolate homologs of Seq ID 3 from other nematode species, and the breadth of the claims drawn to any and all homologs and mutant forms of Seq Id 3 which have not been taught or discussed in the specification, it would have required undue experimentation for one skilled in the art to carry out the claimed methods without a reasonable expectation of success.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 3, 5, 7, 9-11, 15-17, 21-22, 25-32, and 41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "hybridizes" in claim 1 is a relative term which renders the claim indefinite. The term "hybridizes" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Conditions of at least moderate stringency do not sufficiently define the hybridization conditions. It is not clear it the hybridization assay will detect non-specific hybridization. The conditions of hybridization must be included in the claim so that the degree of specific binding can be determined from the claim. Claims 3, 5, 7, 9-11, 15-17, 21-22, 25-32 depend from claim

1.

Claim 1 is indefinite. The language "present it the genome of a nematode" does not convey a clear meaning. It is suggested to rewrite the claim and substitute the term "in" for the term "it".

Claim 5 recites the limitation "isolated molecule" in line1. There is insufficient antecedent basis for this limitation in the claim.

Claims 9-11 recite an indefinite term. Claims 9-11 are rendered indefinite by their recitation of "gene", since there is no clear consensus definition in the art accurately delimiting the metes and bounds of the term "gene" particularly in view of alternative splicing and uncertainties surrounding the metes and bounds of cis-acting sequences regulating mRMA expression.

Claim 41 is indefinite as written. It is not clear exactly what the phrase "expresses such defects" refers to, either the mutant LOV-1 protein or the altered location of vulva and response phenotype. Clarification is required. Also, the claim as written is confusing with regard to exactly which protein, LOV-1 or mutant LOV-1, is encoded by the nucleic acid molecule of claim 1. For example the phrase "a sequence of nucleotides encoding a mutant LOV-1 protein and the LOV-1 protein is encoded by the nucleic acid molecule of claim 1" is ambiguous. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 5, 7, 9-11, 15-17 and 41 are rejected under 35 U.S.C. 102(b) as being anticipated by Wilson et al (Nature, 1994, 368: 32-38).

Claim 1 is directed to an isolated nucleic acid molecule comprising the nucleotide sequence set forth in Seq Id 3, the complement of nucleotide sequence of Seq Id 3, a nucleotide sequence that hybridizes to the nucleotide sequence of Seq Id 3, and that is present in the genome of a nemotode, or a degenerate nucleotide sequence of Seq Id 3. Claim 3 is directed to the same nucleotide sequence that encodes a LOV-1 protein from a nematode. Claim 5 is directed to the same nucleic acid molecule wherein the nucleic acid molecule encodes the amino acid sequence set forth in Seq Id 4. Claim 7 is directed to the same nucleic acid molecule wherein the nucleic acid molecule is derived from C. elegans. Claim 9 is directed to an isolated gene comprising the nucleic acid molecule of claim 1. Claims 10-11 are directed to the same gene wherein the gene comprises transcriptional control sequences that are homologous or heterologous to the encoded gene. Claims 15-17 are directed to isolated nucleic acid molecules that encode mutant forms of the protein of claim 3. Claim 41 is directed to a isolated nucleic acid sequence of the nucleotide sequence set forth in Seq Id 3.

Wilson et al teach C. elegans cosmid clones that comprise over 2.1 Mb of the C. elegans genome. Wilson et al teach a cosmid, (see results of Examiner's sequence search) that has 100% local similarity to the nucleotide sequence set forth in Seq Id 3. Base pair differences at either end of the cosmid represent mutations that are

encompassed in the claims. Thus, the teachings of Wilson et al meet all of the instant claim limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 5, 7, 9-11, 15-17 and 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hughes et al (Nature Genetics, 1995, 10: 151-160) taken with Bargmann et al (ref. AU of the IDS, Science, 1998, 282: 2028-2033) and Wilson et al (Nature, 1994, 368: 32-38).

Hughes et al teach the identification and characterization of the human polycystic kidney disease1 (PKD1). The gene is associated with autosomal dominant polycystic kidney disease (page 151, and throughout entire document). Polycystins are the products of the PKD1 gene. Hughes et al discuss that it would be a challenge to determine the roles of polycystins both in development and in maintaining adult tissues in the kidney and elsewhere (page 159)

Hughes et al do not teach the C. elegans homolog of PKD1.

However at the time the claimed invention was filed, Bargmann et al discuss that C. elegans can be a useful model system for studying gene pathways, particularly the nervous system. Bargmann et al further discuss comparison of the predicted C.

elegans genes with molecules in the vertebrate nervous system reveals many parallels and a few striking differences (page 2028). Bargmann et al further discuss that the C. elegans genome reveals many potential targets for investigation and that C. elegans homologs of highly conserved neuronal genes and human disease genes are open to standard methods for isolating mutations and characterizing gene networks by enhancer and suppressor analysis (page 2032). Accordingly, Wilson et al teach C. elegans cosmid clones that comprise over 2.1 Mb of the C. elegans genome. Wilson et al teach a cosmid, , that has 100% local similarity to the nucleotide sequence set forth in Seq Id 3. Base pair differences at either end of the cosmid represent mutations that are encompassed in the claims.

Accordingly in view of the teachings of Bargmann et al and Wilson et al, it would have been obvious for one of ordinary skill in the art, at the time the invention was made, to use the teachings of Hughes et al to identify a C. elegans homolog of PDK1 in order to elucidate the regulatory pathways of PDK1. One of ordinary skill in the art would have been sufficiently motivated to make such modifications as it was an art recognized goal to elucidate the molecular pathway of polycystic kidney disease in an animal model, particularly *C. elegans* as discussed by Bargmann et al (page 2032 and above).

Thus, the claimed invention, as a whole, is *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claims are allowed. Claims 21-22, 25-32, 42, 49, 74-77, and 82-84 are free of the prior art of record because the prior art of record does not teach or suggest plasmids, vectors, or transgenic nematodes that comprise Seq Id 3 or methods of using same transgenic nematodes to identify new genes. The claims, however, are subject to other rejections.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Kay Pinckney whose telephone number is (703) 305-3553.

Peter Paras, Jr.

Art Unit 1632

JILL D. MARTIN
PATENT EXAMINER